

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
2 June 2005 (02.06.2005)

PCT

(10) International Publication Number
WO 2005/049609 A1

(51) International Patent Classification⁷: C07D 413/06,
401/06, 213/81, A61K 31/4412, 31/537, 31/496, A61P
39/00

(21) International Application Number:
PCT/CA2004/001986

(22) International Filing Date:
18 November 2004 (18.11.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
529657 20 November 2003 (20.11.2003) NZ

(71) Applicant (for all designated States except US): APOTEX
INC. [CA/CA]; 150 Signet Drive, Toronto, Ontario M9L
1T9 (CA).

(72) Inventors; and

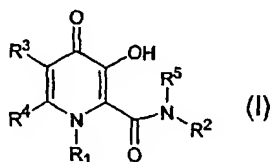
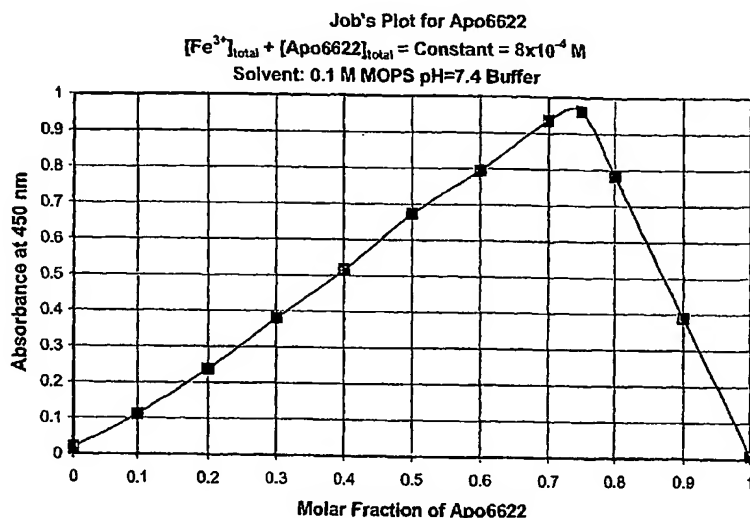
(75) Inventors/Applicants (for US only): TAM, Tim, Fat
[CA/CA]; 155 Veneto Drive, Woodbridge, Ontario L4L
8X6 (CA). SPINO, Michael [CA/CA]; 948 Duncannon
Drive, Pickering, Ontario L1X 2P3 (CA). LI, Wanren
[CA/CA]; 2645 Kipling Avenue, Apt. 1611, Etobicoke,
Ontario M9V 3S6 (CA). WANG, Yingsheng [CA/CA]; 15
Brendwin Road, Toronto, Ontario M6N 4V6 (CA). ZHAO,
Yanqing [CA/CA]; 1875 Steeles Avenue West, Apt. 106,
Toronto, Ontario M3H 5T7 (CA). SHAH, Birenkumar
Hasmukhbhai [IN/CA]; 1130 Wilson Avenue, Apt. #803,
North York, Ontario M3M 1K3 (CA).

(74) Agent: HUGHES, Ivor, M.; Barrister & Solicitor, Patent
& Trademark Agents, 175 Commerce Valley Drive West,
Suite 200, Thornhill, Ontario L3T 7P6 (CA).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,

[Continued on next page]

(54) Title: CYCLOALKYL DERIVATIVES OF 3-HYDROXY-4-PYRIDINONES



of hydrogen and C₁ to C₆ alkyl; R⁵ is selected from the group consisting of hydrogen and C₁ to C₆ alkyl; and its pharmaceutically acceptable salt thereof. Pharmaceutical compositions of such compounds are useful in the removal of excess body iron from patients with iron overload diseases.

(57) Abstract: The present invention provides an cycloalkyl derivative of 3-hydroxy-4-pyridinone which is useful for the chelation of metal ions such as iron. Its preparation and use is described. In particular, the invention concerns the removal of iron in chemical and biological systems including chelating agents having the formula (I); wherein R¹ is X with the proviso that R² is Y; or R¹ is T with the proviso that R² is W; or R¹ is X with the proviso that R² R⁵ N when taken together form a heterocyclic ring selected from piperidinyl, morpholinyl, pyrrolidinyl or piperazinyl, wherein the group piperidinyl, morpholinyl, pyrrolidinyl or piperazinyl is either unsubstituted or substituted with one to three C₁ to C₆ alkyl groups. X is C₃-C₆ cycloalkyl; Y is selected from the group consisting of C₁ to C₆ cycloalkyl; C₁ to C₆ alkyl, and C₁ to C₆ alkyl monosubstituted with a C₃-C₆ cycloalkyl; T is C₁ to C₆ alkyl; W is C₃-C₆ cycloalkyl; R³ is selected from the group consisting of hydrogen and C₁ to C₆ alkyl; R⁴ is selected from the group consisting



CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,

CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

- of inventorship (Rule 4.17(iv)) for US only

Published:

- with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.